

Remarks

Applicants request amendment of the claims as set forth herein. Support for the amendment to Claim 43 is provided by incorporating the definitions from Claim 2 that are necessary to make Claim 43 independent, as well as limitations to R1 previously set forth in original Claim 27. Applicants request amendment of the method of treatment claims to depend from the pending compound claim, and Applicants respectfully request rejoinder of the method of treatment claims commensurate in scope with an allowed compound claim. Applicants hereby reserve the right to file one or more divisional applications to claim non-elected subject matter and subject matter set forth in canceled claims. Claims canceled to the extent that such claims relate to the elected invention have been canceled to expedite prosecution of the present case. Applicants maintain that none of the amendments introduce new matter and the amendments may properly be entered.

Applicants respectfully request entry of the amendments and reconsideration of the rejections in light of the following.

35 USC 102

Claims 2, 35-37, 41, 43-44, and 54 stand rejected under 35 USC 102 (a) and (e) as allegedly being anticipated by Kimura et al. (WO 2003-JP6389 herein referred to as the '389, and in the corresponding family of Mackawana et. al. US 2006/0148858 A1, herein referred to as the '858 application).

The Examiner states that the previously submitted claims were anticipated by the '858 application when R32 was C1-C6alkyloxo and U was an aliphatic linker with one carbon replaced by O. Applicants have now amended the claims to limit the claims to compounds wherein the linker must be substituted and the substituent on the pyrazole ring is limited to hydrogen, methyl, and ethyl. Applicants note that the disclosure of the '858 relating to synthesis of the claimed compounds and preferred groups point to a Ya group that is not substituted. Further, R32, or the corresponding R1 has been amended so that it may no longer be alkyloxo. Applicants respectfully submit that the amended claims obviate the rejection under 102 (a) and (c). Applicants respectfully request reconsideration in light of the requested amendments.

35 USC 103

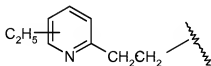
Claims 2, 35-37, 41, 43-44, 54, 68, and 69 are rejected under 35 USC 103 (a) as allegedly unpatentable over the '858 application.

Applicants respectfully disagree. Applicants note that the claims have been amended, and submit that the differences between the prior art and the claims of the instant case are non-obvious in light of the broad disclosure of the '858 application.

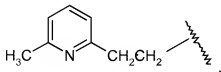
The Examiner states that Claims 68 and 69 differ from the 858 application by H, CH₃ vs. –Pr, or Et. Applicants respectfully note that there are multiple changes from the cited molecules. In each instance, the presently claimed compounds have a substituted linker region. The '858 patent application discloses a synthesis process and focuses the artisan to pyrazole like compounds having no substituents in the linker region of the molecule. The required alkyl substitution in the linker region to provide PPAR delta activity is an unexpected advance in the art.

Further, Applicants note that one of the cited compounds is both a position isomer as well as a compound requiring, and seeming to prefer a propyl substituent on the pyrazole ring. All of the present claims are now further limited and exclude all such propyl substituents, as well as requiring substitution in the linker region of the molecule. Finally, in contrast, the preferred substitution on the pyrazole ring of the presently claimed compounds is a methyl group.

Applicants submit that particularly in light of the requested amendments, the presently claimed compounds are at least as surprising as the compounds deemed non-obvious in Takeda. As Applicants previously noted, a recent decision by the U.S. Court of Appeals for the Federal Circuit in Takade Chemical v. Alphapharm, 492 F.3d 1350, 83 U.S.P.Q.2D 1169 (C.A.F.C. 2007). The issue before the court was whether a chemical moiety having a structural formula (i):



Should be considered obvious in view of prior disclosure of a chemical moiety having structural formula (2):



where both moieties were disclosed to have similar, albeit not identical, biological activities. The court affirmed the finding of non-obviousness by a district court.

The court began by noting that:

[i]n addition to structural similarity between the compounds, a prima facie case of obviousness also requires a showing of “adequate support in the prior art” for the

change in structure. (492 F.3d 1350 at 1356, quoting *In re Grabiak*, 769 F.2d 729, 731-32 (*Fed. Cir.* 1985). Emphasis added.

The court noted that

[a] known compound may suggest its homolog, analog, or isomer because such compounds “often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties.” *Id.*

However, the court clarified that:

[...] in order to find a prima facie case of unpatentability in such instances, a showing that the “prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention” was also required. *Id.* (citing *In re Jones*, 958 F.2d 347 (*Fed. Cir.* 1992); *Dillon*, 919 F.2d 688; *Grabiak*, 769 F.2d 729; *In re Lahu*, 747 F.2d 703 (*Fed. Cir.* 1984). Emphasis added.)

Applicants maintain that the narrow genus of compounds claimed by this application is surprising and non-obvious, particularly in the chemical arts where pharmacological activity related to chemical modifications may be particularly unpredictable. Applicants respectfully submit that the ‘389 and ‘858 applications fail to satisfy the guidelines set forth in *Takeda*, and the present rejection may properly be withdrawn.

Applicants were not able to identify a teaching in the art to direct the skilled artisan to select the cited CAS RN628335-96-6 and RN628334-65-6. Even if the skilled artisan were to select these two compounds, Applicants maintain that the artisan would further require a teaching or motivation modify these particular compounds, in a manner that is outside the genus of the incredibly broad ‘858 application, to provide the presently claimed compounds. Applicants respectfully note that the art must be considered without the use or benefit of Applicants’ specification to create a view of the art that relies upon improper hindsight reconstruction. There must be some suggestion, teaching, or motivation in the prior art to select the particular compounds, and then to direct the artisan to prepare the new compounds that have different structure than the compounds available in the art.

Finally, although the Examiner states that one must necessarily use hindsight in the obviousness analysis, Applicants submit that the obviousness analysis requires the Examiner to return to the time the invention was made, without the benefit disclosure of the presently claimed invention. The Examiner must view the prior art without reading the patent’s teachings into the prior art. *Vandenberg v Dairy Equip. Co.*, 740 F.2d 1560, 224 USPQ195 (*Fed. Cir.* 1984). Applicants maintain that drawing knowledge of the present invention, when the prior art does not

contain or suggest that knowledge, is to use the invention as a template for its own reconstruction, is an inappropriate process by which to determine patentability. The invention must be viewed not after the blueprint has been drawn by the inventor, but as it would have been perceived in the state of the art that existed at the time the invention was made. *Sensonics Inc. v. Aerosonic Corp.*, 81 F3d 1566, 38 USPQ2d 1551, 1554 (*Fed. Cir.* 1996). Further, as recently confirmed by Takeda: “it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner.” (492 F.3d 1350 at 1356 and 1357). Applicants have not identified any teaching in the ‘389 or ‘858 applications to direct the skilled artisan chemist to prepare the compounds having branched aliphatic linker or the need to do so.

Applicants submit that the test for chemical obviousness delineated in Takeda has not been satisfied by the general disclosure of the ‘389 and ‘858 application. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Conclusion

Applicants request entry of the amendments and prompt favorable consideration in light of the above. If the Examiner deems that the claims are not in condition for allowance, then Applicants respectfully request a prompt advisory action to facilitate prosecution of the application.

The Examiner is asked to contact the undersigned attorney for any matters relating to this application.

Respectfully submitted,

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